



UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/147,693	02/17/99	LUBITZ	W P564-9005

HM12/0518
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EXAMINER
SANDALS, W

ART UNIT	PAPER NUMBER
1636	15

DATE MAILED: 05/18/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Advisory ActionApplication No.
09/147,693Applicant(s)
Lubitz et al.Examiner
WILLIAM SANDALSArt Unit
1636

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED May 10, 2001 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid the abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

THE PERIOD FOR REPLY [check only a) or b)]

- a) ☒ The period for reply expires 5 months from the mailing date of the final rejection.
- b) ☐ In view of the early submission of the proposed reply (within two months as set forth in MPEP § 706.07 (f)), the period for reply expires on the mailing date of this Advisory Action, OR continues to run from the mailing date of the final rejection, whichever is later. In no event, however, will the statutory period for the reply expire later than SIX MONTHS from the mailing date of the final rejection.

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☐ A Notice of Appeal was filed on _____. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.
2. ☐ The proposed amendment(s) will be entered upon the timely submission of a Notice of Appeal and Appeal Brief with requisite fees.
3. ☒ The proposed amendment(s) will not be entered because:
- (a) ☒ they raise new issues that would require further consideration and/or search. (See NOTE below);
- (b) ☐ they raise the issue of new matter. (See NOTE below);
- (c) ☒ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
- (d) ☐ they present additional claims without cancelling a corresponding number of finally rejected claims.

NOTE: See attached.

4. ☐ Applicant's reply has overcome the following rejection(s): _____
5. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment cancelling the non-allowable claim(s).
6. ☐ The a) ☐ affidavit, b) ☐ exhibit, or c) ☐ request for reconsideration has been considered but does NOT place the application in condition for allowance because: _____
7. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.
8. ☒ For purposes of Appeal, the status of the claim(s) is as follows (see attached written explanation, if any):
- Claim(s) allowed: _____
- Claim(s) objected to: _____
- Claim(s) rejected: 38-76
9. ☐ The proposed drawing correction filed on _____ a) ☐ has b) ☐ has not been approved by the Examiner.
10. ☐ Note the attached Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
11. ☐ Other: _____



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DEA/FCE-1994

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09/147,693			

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Please find below a communication from the EXAMINER in charge of this application

Commissioner of Patents

Response to Arguments

1. Arguments set forth in Paper No. 14, filed May 10, 2001 assert that the Pakula et al. reference has been misinterpreted. It is asserted that, rather than discussing the thermostability of the operator/repressor complex, Pakula et al. discuss the thermostability of the Cro repressor. The first line of the Final Office Action rejection refers to the fact that the teachings of Pakula et al. are directed to the thermostability of the repressor protein. Pakula et al. teaches important general knowledge of those of ordinary skill in the art regarding the basic thermodynamics of molecular binding, and its general results on the thermostability of a DNA/repressor binding complex. Repressor protein binding to the operator DNA sequences must follow the laws of thermodynamics that are well set forth in Pakula et al. Pakula et al. does teach that the binding affinity of a repressor protein to lambda operator sequences is affected by changes in the lambda operator DNA sequence. Pakula et al. teaches that the thermostability of the operator/DNA complex is altered by changes in the binding affinity. This is well known information regarding the

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thermodynamics of protein/DNA binding. Stronger binding affinity results in higher thermostability of the complex will be and weaker binding affinity results in lower thermostability. The lesson taught by Pakula et al. is basic to the understanding of the physical principles of molecular interaction.

2. Arguments set forth in Paper No. 14 assert that Benson et al. did not teach mutated operator sequences having increased thermostability. Referring to the discussion above, Benson taught that repressor bound to mutated operator DNA sequences with different affinities with respect to the changes in the DNA sequence. The different binding affinities of the mutated operator sequences must result in different thermal stabilities of the repressor/operator complex. The fact that Benson et al. does not mention thermostability is irrelevant to the basic physical principles which underlie the binding affinities. Requiring Benson et al. to specifically mention this fact is not necessary to make the point, since the physical principals must apply in all cases.
3. Arguments set forth in Paper No. 14 assert that US 5,576,190 taught "tighter regulation" at column 7, lines 11-20. As pointed out in the Final Office Action, column 10, (lines 48-49) "pHDM159 contains a change that increases the binding affinity for the cI857 repressor". As above, changes in the binding affinity must also affect the thermostability of the complex.
4. Proposed amendments to claim 38 have been set forth as "further distinguishing" from the teachings of Chen et al. The proposed claim amendments raise new issues which would require a new search. Chen et al. provides basic teachings regarding the claimed invention which are relevant, and the "further distinguishing" from Chen et al. while raising new issues, does not simplify the issues of the rejection. Chen et al. taught mutated operator sequences in a vector which were used in conjunction with the cI857 repressor to control gene expression in a temperature dependent fashion, albeit, the mutated sequences were discovered from naturally occurring mutation events and not made by a mutation protocol.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to William Sandals whose telephone number is (703) 305-1982. The examiner can normally be reached on Monday through Friday from 9:30 AM to 6:00 PM.

May 16, 2001


TERRY MCKELVEY
PRIMARY EXAMINER